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control group. The morbidity at the time of the outbreak was 10 percent in the treatment group and 90 percent in the control group. The mortality was 5.2 percent in the control group and 2.1 percent in the treatment group. The controls required follow-up treatment with antibiotics two weeks after the outbreak and the treatment group did not require any mass medication with antibiotics.

IN THE ABSTRACT

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A readily water-soluble ingestible form of ketoprofen is provided by the reaction of ketoprofen and any edible weak base to yield a palatable, stable, safe pharmaceutical solution for mass medication of animals. Any edible weak base such as sodium bicarbonate may be used with ketoprofen in a ratio of 10 to 1 by weight.

No new matter is added by the foregoing amendments.

REMARKS

Favorable reconsideration of this application is respectfully requested. Claims 1-20 are pending in this application.

Applicants have amended claims 2, 19, and 20, the abstract and the specification. The amended claims are supported by the specification or drawings, and thus, do not constitute new matter. The amended abstract and specification are merely the correction of typographical errors, and thus, does not constitute new matter. Claims 1-20 are presented for examination.

35 U.S.C. § 112, SECOND PARAGRAPH REJECTION OF CLAIMS 2 and 20

Claims 2 and 20 stand rejected under 35 U.S.C. § 112, second paragraph. As amended, the lack of antecedent basis has been corrected in claim 2. Additionally, as amended, claim 20 is no longer a flavoring agent depending from a claim directed to a method. Thus, Applicants respectfully request the rejection of claims 2 and 20 be withdrawn.

35 U.S.C. § 102(b) REJECTION OF CLAIMS 1 and 12

In the Office Action, claims 1 and 12 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Dondi *et al.*, U.S. Patent No. 5,624,682 (Dondi). Applicants respectfully traverse this rejection.

Dondi discloses a pharmaceutical formulation based on a ketoprofen formulation in soft capsules (Dondi, Title, Column 1 line 34, Column 2 lines 9, 50 and 67, Column 3 lines 8 and 30, Column 4 line 2, and Claim 1). These soft capsules are clearly intended for use by humans. In fact, Dondi's invention is limited to use in soft capsules.

Dondi's invention is very different from the present invention, which is directed to a pharmaceutical solution for oral medicating of animals. Nowhere in Dondi is there any suggestion or teaching that the pharmaceutical formulation can be used to treat animals. As such, Dondi fails to disclose a pharmaceutical solution for treatment of animals. More specifically, Dondi fails to disclose a pharmaceutical solution comprising ketoprofen and an edible base for oral medicating of animals. Accordingly, Dondi fails to disclose the invention as claimed by claims 1 and 12.

In order to anticipate, a reference must teach each and every element of a claim. Applicants respectfully submit that the indicated differences show that the present claims are not anticipated by Dondi. Accordingly, for the above-identified reason, the rejection under 35 U.S.C. § 102(b) should be withdrawn.

ADDITIONAL 35 U.S.C. § 102(b) REJECTION OF CLAIMS 1

In the Office Action, claim 1 was further rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Daher, U.S. Patent No. 5,348,745 (Daher). Applicants respectfully traverse this rejection.

Daher discloses a method of producing pharmaceutical tablets i.e., pills (Daher, Title, Abstract, Field of the Invention, Column 1 line 34, Column 2 lines 24-26, 40 and 56, Column 3 lines 16 and 42, Column 4 line 68, Column 5 line 49, Column 6 lines 24-34, Column 7 line 4 and 60, Column 8 lines 15-20, Column 11 lines 22, 40 and 50-64, Column 13 lines 3 and 4, Column 14 line 22, Column 15 lines 16 and 34 and Claim 3). Conversely, the claimed invention as recited by claim 1 is for a pharmaceutical solution. Nowhere in Daher is there a teaching or suggestion of a pharmaceutical solution for administration to an animal. In fact, Daher teaches the opposite of the applicant's invention. Daher teaches the formulation of a tablet from

an aqueous solution. Indeed, tablets and solutions are utilized in completely different treatment regimens. Therefore it is respectfully submitted that the claimed invention as recited by claim 1 is distinguishable over Daher.

In order to anticipate, a reference must teach each and every element of a claim. Applicants respectfully submit that the indicated differences show that the present claims are not anticipated by Daher. Accordingly, for the above-identified reason, the rejection under 35 U.S.C. § 102(b) should be withdrawn.

35 U.S.C. § 103(a) REJECTION OF CLAIMS 1, 5-13, and 17

In the Office Action, claims 1, 5-13, and 17 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Dondi. Applicants respectfully traverse this rejection.

Claim 1 recites, *inter alia*, an oral medication for animals. Claim 5-12 recites, *inter alia*, a method for the treatment of a disease in an animal. Claim 12 recites, *inter alia*, a method for the analgesic treatment of an animal comprising administering to said animal a pharmaceutically effective amount of the ketoprofen solution of claim 1.

For at least the reasons stated above, Dondi fails to teach or suggest a pharmaceutical solution as recited in claims 1 and 5-12. In this regard, Dondi discloses a method of producing a soft gelatin capsule. The Dondi disclosure of soft gelatin capsules, pills, tablets, etc. is not an effective means of treating animals. Specifically, treating animals with capsules requires the handling of each and every animal. Dondi further discloses the amount of ketoprofen per capsule to be between 25 and 50 mg. This amount of ketoprofen is clearly not meant to treat animals. For example, at a typical dosage of 1-2 mg/kg, a typical 350 kg cow would require 7-28 capsules. Treating captive animals in this manner is, at least, burdensome if not impossible. Thus, besides failing to disclose the claimed pharmaceutical solution, Dondi fails to disclose a method of medicating animals.

Claim 13 recites, *inter alia*, a pharmaceutical solution comprising ketoprofen and an edible weak base, wherein ketoprofen is present in an amount of 1-10% by weight of the solution and wherein the edible base is present in an amount no greater than about 90% by weight of the solution. Claim 17 recites, *inter alia*, the pharmaceutical solution comprising ketoprofen and an edible weak base, wherein ketoprofen is present in an amount of 10-20% by weight of the solution and wherein

the edible base is present in an amount no greater than about 80% by weight of the solution.

The legal concept of *prima facie* obviousness allocates who has the burden of going forward with production of evidence in each step of the examination process. *See* the *Manual of Patent Examining Procedure* (MPEP) 2142. "If the Examiner does not produce a *prima facie* case, the Applicant is under no obligation to submit evidence of non-obviousness." *See* MPEP 2142. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The MPEP expressly requires each of elements these in 706.02(j), *see also* MPEP 2143.

The cited reference does not satisfy a finding of obviousness for at least the following reasons: First, there is no suggestion or motivation provided for one of ordinary skill in the art to use the teachings of, or modify, this reference for preparing or using a pharmaceutical solution comprising ketoprofen and an edible base for oral administration to animals. Dondi is instead directed to a pharmaceutical formulation for soft capsules. Second, there is no reasonable expectation that the pharmaceutical formulation disclosed in Dondi may be used to treat animals. Finally, Dondi fails to teach or suggest the claimed limitation of oral treatment of animals.

In sum, the Dondi reference fails to teach, provide motivation, or disclose any suggestion related to preparing or using a pharmaceutical solution comprising ketoprofen and an edible base for oral administration to animals. Without suggestion or motivation to modify Dondi, the claims are not rendered obvious. *See* MPEP 706.02(j)(D).

ADDITIONAL 35 U.S.C. § 103(a) REJECTION OF CLAIMS 1-20

Claims 1-20 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Daher. Applicants respectfully traverse this rejection.

As discussed above, "If the Examiner does not produce a *prima facie* case, the Applicant is under no obligation to submit evidence of non-obviousness." *See* MPEP 2142. To establish a *prima facie* case of obviousness, three basic criteria must be met.

First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The MPEP expressly requires each of elements these in 706.02(j), *see also* MPEP 2143.

The cited reference does not satisfy a finding of obviousness for at least the following reasons: First, there is no suggestion or motivation provided for one of ordinary skill in the art to use the teachings of, or modify, this reference for preparing or using a pharmaceutical solution comprising ketoprofen and an edible base for oral administration to animals. Daher is instead directed to a the formulation of a tablet comprising an edible organic acid. Second, the Office Action provides no support or evidence that the teaching of Daher would work in the environment of oral medicating animals and thus satisfy the intended purpose of the Applicants' invention. Therefore, the disclosure of Daher is counter to, and in fact teaches away from the present invention as recited by claims 1-20. Finally, Daher fails to teach or suggest the claimed limitation of oral treatment of animals.

Furthermore, there is no teaching or suggestion that the pharmaceutical mixture may be used to treat animals. Specifically, the tablets disclosed by Daher, in a manner similar to the soft capsules disclosed by Dondi, are not suitable for the treatment of animals. Therefore, it would not be obvious to one skilled in the art to use the discloser of Daher to treat animals. Nowhere in Daher is there a teaching or suggestion of a pharmaceutical solution for oral administration to animals. Indeed, Daher teaches away from the applicant's invention as it teaches the formulation of a tablet from an aqueous solution. The teaching of Daher is in sharp contrast to the present invention which is a pharmaceutical solution. Certainly, pills and solutions are utilized in completely different treatment regimens. Therefore, it is respectfully submitted that the claimed invention as recited by claims 1-20 is distinguishable over Daher.

Finally, the Daher reference fails to teach, provide motivation, or disclose any suggestion related to preparing or using a pharmaceutical solution comprising ketoprofen and an edible base for oral administration to animals. Without suggestion or motivation to modify Daher, the claims are not rendered obvious. *See* MPEP 706.02(j)(D). Therefore, it is respectfully submitted that it would not be obvious to

one skilled in the art to use the disclosure of Daher to practice the present invention. Thus, Applicants respectfully request that the rejection of claims 1-20 be withdrawn.

CONCLUSION

As all of the outstanding rejections have been addressed and all of the claims are believed to be in condition for allowance, the Applicants respectfully requests a Notice of Allowability. Minor typographical errors in the claims, specification, and abstract have been corrected. The Examiner is invited to contact the undersigned representative should any further issues arise.

Respectfully submitted,
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Dated: June 17, 2002

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MARKED-UP VERSION TO SHOW CHANGES MADE

IN THE CLAIMS

2. The pharmaceutical solution of claim1, wherein the edible [weak] base is selected from the group consisting of sodium bicarbonate, sodium chloride, potassium chloride, sodium sulfate, and potassium sulfate.

19. A method for preparing a water-soluble ingestible form of ketoprofen [eomprising] comprising the following steps:

(a) mixing ketoprofen and an edible weak base in a ratio of 1:10 by weight;

(b) adding a flavoring agent.

20. The method of claim 19, wherein said flavoring agent [of claim 19, wherein said flavoring agent] is selected from the group consisting of cyclohexyl-sulfamic acid, saccharin (o-benzosulfimide), Aspartame (i.e., L-Aspartyl-L-phenylalanine methyl ester), and sugar.

IN THE SPECIFICATION

Page 3, the paragraph beginning at line 31 has been amended as follows:

Bull. Soc.Vet.Prat.de France, 7/90, T. 74, No.7, P. 377 describes the use of ketoprophene as analgesic therapy in the [treatement] treatment of equine colic (administered intravenously). A dosage of 2 mg per kg or 2 mL of 10% [Ketofen] Ketoprofen solution per 100 kg was used.

Page 4, the paragraph beginning at line 7 has been amended as follows:

There is a need for stable liquid forms of ketoprofen that can be orally administered (i.e., ingested) via an animal's drinking water without rejection by the animal because of the bad taste imparted by the liquid ketoprofen. Such a palatable form of ketoprofen allows large scale dosage-controlled treatment of animals with the [antiobiotic] antibiotic.

Page 5, the paragraph beginning at line 8 has been amended as follows:

[A 2] Two 1000 head Finishing Barn [Site] Sites experienced an outbreak of swine influenza. Both barns, which housed 150 pound finishing hogs, experienced the outbreak simultaneously. We used one barn as the treatment group and one as the control group. The treatment group was given 1 mg/pound of Ketoprofen for 3 days orally through the drinking water and the control group was given a placebo of Flavored Sodium Bicarbonate in the water. We observed the pigs until they were marketed at 260 pounds 8 to 10 weeks after the outbreak. The results of the study included an average time to market for the treatment group of 9 days less than the control group. The morbidity at the time of the outbreak was 10 percent in the treatment group and 90 percent in the control group. The mortality was 5.2 percent in the control group and 2.1 percent in the treatment group. The controls required follow-up treatment with antibiotics two weeks after the outbreak and the treatment group did not require any mass medication with antibiotics.

IN THE ABSTRACT

A readily water-soluble ingestible form of ketoprofen is provided by the reaction of ketoprofen and any edible weak base to [yeild] yield a palatable, stable, safe pharmaceutical solution for mass medication of animals. Any edible weak base such as sodium bicarbonate may be used with ketoprofen in a ratio of 10 to 1 by weight.